

1                    RADIOACTIVE THERAPEUTIC SEED HAVING  
2                    SELECTIVE MARKER CONFIGURATION  
3

4            This application is a continuation of Serial No. 10/295,658,  
5    filed November 15, 2002, to be issued as U.S. Patent Number  
6    6,717,752, which is a continuation of Serial No. 09/514,787, filed  
7    February 28, 2000, now issued as U.S. Patent No. 6,482,143, which  
8    is a continuation-in-part of U.S. Serial No. 09/371,243, filed  
9    August 10, 1999, now issued as U.S. Patent No. 6,200,258, all of  
10   which are hereby incorporated by reference herein in their  
11   entirety.  
12

13                    BACKGROUND OF THE INVENTION  
14

15    1. Field of the Invention

16            The invention relates to radioactive therapeutic seeds. More  
17    particularly, the invention relates to improved radioactive  
18    therapeutic seeds for the treatment of oncological and other  
19    medical conditions.  
20

21    2. State of the Art

22            Radioactive seed therapy is a well known and well accepted  
23    medical procedure for the treatment of various oncological and  
24    other medical conditions. Seed therapy, also known as

1 brachytherapy typically involves the implantation of one or more  
2 tiny capsules (seeds) into or around a treatment site. The  
3 capsules contain a radioactive isotope that irradiates the  
4 treatment site at close range without adversely affecting other  
5 parts of the body. Brachytherapy has been used successfully in  
6 the treatment of various types of cancers such as prostate cancer.  
7 It has also been used to prevent the growth or regrowth of tissues  
8 in the treatment of various occlusive diseases such as  
9 arteriosclerosis and arthrosclerosis subsequent to balloon  
10 angioplasty.

11  
12       Radioactive therapeutic seeds are carefully designed to  
13 possess several important qualities. First, they are relatively  
14 small, typically approximately 0.025 inch in diameter and  
15 approximately 0.16 inch long, so that they may be implanted using  
16 minimally invasive instruments and techniques. Second, the  
17 radioactive isotope must be enclosed in a biocompatible protective  
18 package since the seeds are typically not removed and will remain  
19 in the body for many years. Third, the isotope should be  
20 positioned within the protective package so as to avoid any "hot  
21 spots" of radiation. Fourth, each seed preferably includes a  
22 radiopaque (e.g. high Z material) marker so that it can be located  
23 at the treatment site with the aid of fluoroscopy. Fifth, the  
24 protective package and the radiopaque marker are preferably

1 configured such that each does not cast "shadows" in the  
2 irradiation pattern of the isotope.

3  
4 The state of the art of radioactive therapeutic seeds is  
5 substantially disclosed in seven U.S. Patents: Number 5,713,828  
6 to Coniglione for "Hollow-Tube Brachytherapy Device", Number  
7 5,405,309 to Carden, Jr. for "X-Ray Emitting Interstitial  
8 Implants", Number 4,891,165 to Suthanthiran for "Device and Method  
9 for Encapsulating Radioactive Materials" and Number 4,784,116 to  
10 Russell, Jr. et al. for "Capsule for Interstitial Implants",  
11 Number 4,702,228 to Russell, Jr. et al. for "X-Ray Emitting  
12 Interstitial Implants", Number 4,323,055 to Kubiadowicz for  
13 "Radioactive Iodine Seed", and Number 3,351,049 to Lawrence for  
14 "Therapeutic Metal Seed Containing within a Radioactive Isotope  
15 Disposed on a Carrier and Method of Manufacture".

16  
17 The Lawrence patent describes many of the essential features  
18 of radioactive therapeutic seeds. Lawrence describes radioactive  
19 isotopes (I-125, Pd-103, Cs-131, Xe-133, and Yt-169) which emit  
20 low energy X-rays and which have relatively short half-lives.  
21 Once implanted at a treatment site, these isotopes provide  
22 sufficient radiotherapy without posing a radiation danger to the  
23 medical practitioner(s), people in the vicinity of the patient, or  
24 other parts of the patient's body. Lawrence further describes a

1 protective capsule which contains the isotope and prevents it from  
2 migrating throughout the body where it might interfere with  
3 healthy tissue. The capsule is cylindrical and made of low atomic  
4 number biocompatible materials such as stainless steel or titanium  
5 which substantially do not absorb X-rays. The isotope is coated  
6 on a rod shaped carrier made of similar X-ray transparent (e.g.  
7 low Z) material and is placed inside the capsule cylinder. The  
8 ends of the capsule cylinder are closed by swaging or spinning and  
9 soldering or welding. According to a preferred embodiment,  
10 Lawrence places a radiopaque marker inside the seed. In one  
11 embodiment, the marker is a wire embedded inside the carrier rod.  
12 The wire is made of high atomic number material such as gold or  
13 tungsten which absorb X-rays.

14  
15 Kubiadowicz made a minor improvement in the basic Lawrence  
16 design by providing that the entire isotope carrier be made of  
17 radiopaque material such as silver. Kubiadowicz recognized that  
18 since the isotope was carried on the entire outer surface of the  
19 carrier, there was no need to make the carrier body X-ray  
20 transparent as suggested by Lawrence. The larger radiopaque  
21 carrier body described by Kubiadowicz makes the seeds easier to  
22 see with X-ray or fluoroscopic examination. Thus, the seeds may  
23 be placed more accurately at or around the treatment site.

1       The Coniglione patent provided a tubular seed adapted for  
2 longitudinally receiving suture material to facilitate securing  
3 the seed at an implant site. The seed optionally includes a  
4 radiopaque band centrally located on the outer surface of the  
5 seed, and the radioactive isotope either extends over the entire  
6 outer surface of the seed, including over the band, or is coated  
7 on the outer surface of the seed from the ends of the seed to  
8 areas adjacent the edges of the band.

9  
10       Despite the fact that radioactive therapeutic seeds have been  
11 in use for over thirty years and despite the several significant  
12 improvements made in these seeds, many concerns still exist  
13 regarding their design. In certain instances where radioactive  
14 seed therapy is prescribed for a patient, a physician may desire  
15 to have different levels of radioactivity at various locations  
16 within the treatment site and thereafter monitor how the tissue is  
17 affected by seeds radiating particular levels of radiation. Or  
18 the physician may want to implant seeds having isotopes with  
19 different half lives, thereby permitting selected locations to  
20 receive radiation over a longer period of time, and monitor which  
21 seeds are active. However, according to the known seed designs  
22 and methodology, it is not possible to distinguish one seed from  
23 another after implantation based upon a seed marker with an  
24 imaging systems, e.g., X-ray. Due to the indistinguishability of

1 the seeds, implantation of seeds having different respective  
2 properties at a single site of treatment is not purposefully  
3 performed.

4  
5 SUMMARY OF THE INVENTION  
6

7 It is therefore an object of the invention to provide a  
8 system of radioactive therapeutic seeds in which at least one of  
9 the therapeutic seeds has a different level of radioactivity  
10 relative to other seeds.

11  
12 It is also an object of the invention to provide a system of  
13 radioactive therapeutic seeds in which at least one of the  
14 therapeutic seeds has a marker which is different relative to  
15 other seeds.

16  
17 It is another object of the invention to provide radioactive  
18 therapeutic seeds in which at least one of the therapeutic seeds  
19 has a different level of radioactivity and/or different half-life  
20 relative to other seeds and the marker in the at least one  
21 therapeutic seed indicates the different level of radioactivity  
22 and/or half-life relative to the other seeds.

1        It is an additional object of the invention to provide  
2 radioactive therapeutic seeds in which different seeds are  
3 provided with markers of different size which indicate their  
4 respective levels of radioactivity or half-life.

5  
6        It is yet another object of the invention to provide a  
7 radioactive therapeutic seed which is adapted to receive markers  
8 of various lengths by a physician just prior to insertion.

9  
10       It is yet a further object of the invention to provide a  
11 radioactive therapeutic seed which is adapted to have a marker  
12 which can be selectively configured by a physician just prior to  
13 insertion.

14  
15       In accord with these objects which will be discussed in  
16 detail below, the radioactive therapeutic seeds of the present  
17 invention include a carrier structure bearing a radioactive  
18 isotope and a radiopaque marker.

19  
20       According to a first embodiment of the invention, the isotope  
21 bearing structure may be one or more radiolucent particles,  
22 preferably made from titanium, aluminum or glass, and preferably  
23 spherically shaped. The particles are provided with a thin  
24 coating of silver to facilitate the adhesion of the isotope

1 thereto. Also provided is a relatively thick tubular titanium  
2 plug having an axial first radiopaque marker therein. The plug  
3 preferably includes a circumferential ridge against which the open  
4 ends of the two halves of the capsule are butt against and welded  
5 thereto. The plug and the marker are provided with a transverse  
6 bore accessible from the exterior of the seed. A second marker  
7 may be positioned in the bore, thereby radiographically  
8 distinguishing a seed provided with the second marker relative to  
9 a seed not provided with the second marker; i.e., a seed provided  
10 with solely the first marker will have a broken linear  
11 radiographic image, while a seed provided with both the first and  
12 second markers will have a cross-shaped radiographic image. A  
13 plurality of seeds as described may be provided in a system which  
14 includes a plurality of seeds and a plurality of second markers  
15 for selective insertion into the seeds by a physician.  
16 Alternatively, the seeds may be provided to the physician already  
17 divided into groups which are distinguishably radiographically  
18 marked.

19  
20 According to a second embodiment of the invention, a seed  
21 includes an isotope bearing structure, which is preferably a pair  
22 of silver tubes having an interior surface on which the isotope is  
23 provided. One silver tube is positioned in each half of the  
24 capsule, and the halves of the capsule are welded about a

1 relatively thick centrally located tubular titanium plug. The  
2 plug is preferably provided with a first radiopaque marker  
3 therein. The plug and the marker are provided with a transverse  
4 bore accessible from the exterior of the seed, and the bore may be  
5 provided with a second marker, as described above. In addition,  
6 the isotope bearing tube is preferably smaller than the interior  
7 of each half of the capsule, and a spacer is preferably provided  
8 in each half of the capsule between the tube and the plug to  
9 prevent relative movement of the tube within the capsule.

10  
11 According to a third embodiment of the invention, the isotope  
12 is deposited on the outer surface of a hollow radiolucent tube. A  
13 radiopaque band may be centrally located on the outer surface of  
14 the seed, and the radioactive isotope may then either extend over  
15 the entire outer surface of the seed, including over the band, or  
16 may be coated on the outer surface of the seed from the ends of  
17 the seed to areas adjacent the edges of the band. A biologically-  
18 compatible, radiolucent, surface-sealing layer seals the external  
19 surface of the tube. A radiopaque marker wire is positioned in  
20 the hollow of the tube, and where the seed is provided with a  
21 radiopaque band, the marker wire is preferably of a length  
22 different than the band. It will be appreciated that in a system  
23 of seeds according this embodiment, seeds may be radiographically

1 distinguished from one another by providing seeds with marker  
2 wires of different lengths.

3  
4 According to a fourth embodiment of the invention, the seed  
5 includes an element on which the isotope is provided, and a marker  
6 which can be varied in size or shape by application of energy to  
7 the seed.

8  
9 According to fifth through ninth embodiments of the  
10 invention, the seed includes a substantially cylindrical outer  
11 member, and a substantially cylindrical inner member provided  
12 within the outer member and having two large diameter portions and  
13 a relatively smaller diameter portion therebetween. A marker  
14 which permits at least one of a radiographic and a MRI image is  
15 longitudinally disposed within the inner member, and a radioactive  
16 isotope is carried on the small diameter portion of the inner  
17 member. In each embodiment, the marker may be drilled to a  
18 smaller size, e.g., with a laser drill or mechanical drill, to  
19 radiographically distinguish the drilled marker from a non-drilled  
20 marker.

21  
22 Each embodiment permits at least two groups of seeds to be  
23 radiographically distinguished from one another by the use of  
24 differing marker configurations. Each embodiment is further

1 capable of being selectively marked by the physician prior to  
2 implantation of the seeds, or by the manufacturer for delivery to  
3 the physician in radiographically distinguishable sets. As a  
4 result, seeds having different levels of radiation emission can be  
5 distinguished in vivo and their effect monitored by the physician.

6  
7 Additional objects and advantages of the invention will  
8 become apparent to those skilled in the art upon reference to the  
9 detailed description taken in conjunction with the provided  
10 figures.

11  
12 BRIEF DESCRIPTION OF THE DRAWINGS

13  
14 Figure 1 is an enlarged schematic longitudinal section of a  
15 radioactive therapeutic seed according to a first embodiment of  
16 the invention;

17  
18 Figure 2 is a view similar to Figure 1 with the seed axially  
19 rotated by 90° relative to the view shown in Figure 1;

20  
21 Figure 3 is a view similar to Figure 1 with the radioactive  
22 therapeutic seed according to a first embodiment of the invention  
23 shown with a secondary marker provided therein;

1        Figure 4 is a view similar to Figure 3 with the seed axially  
2        rotated by 90° relative to the view shown in Figure 3;

3  
4        Figure 5 is an enlarged schematic longitudinal section of a  
5        radioactive therapeutic seed according to a second embodiment of  
6        the invention;

7  
8        Figure 6 is a view similar to Figure 5 shown with the seed  
9        axially rotated by 90° relative to the view shown in Figure 5;

10  
11       Figure 7 is a view similar to Figure 5 with the radioactive  
12       therapeutic seed according to a first embodiment of the invention  
13       shown with a secondary marker provided therein;

14  
15       Figure 8 is a view similar to Figure 7 shown with the seed  
16       axially rotated by 90° relative to the view shown in Figure 7;

17  
18       Figure 9 is an enlarged schematic longitudinal section of a  
19       radioactive therapeutic seed according to a third embodiment of  
20       the invention shown with a wire marker having a first length;

21  
22       Figure 10 is a view similar to Figure 9 shown with a wire  
23       marker having a second length different than the first length;

Figure 11 is a view similar to Figure 9 shown with two tubular co-axial markers;

Figure 12 is an enlarged schematic longitudinal section of a radioactive therapeutic seed according to a fourth embodiment of the invention shown with a marker having a first shape;

Figure 13 is a view similar to Figure 12 with the marker having a second shape;

Figure 14 is an enlarged schematic longitudinal section of a radioactive therapeutic seed which is thereafter modified in accord with the fifth embodiment of the invention;

Figure 15 is a view similar to Figure 14 in which the seed of Figure 14 is modified by providing a longitudinal bore therein and a marker in the bore according to the fifth embodiment of the invention;

Figure 16 is a view similar to Figure 15 in which the marker has been altered in size to indicate a differing level of radioactivity of the seed relative to a marker unaltered in size;

1        Figure 17 is a view similar to Figure 15 in which the seed is  
2 provided with a lumen and marker therein according to a sixth  
3 embodiment of the invention;

4  
5        Figure 18 is an enlarged schematic longitudinal section of a  
6 first manufactured portion of a radioactive therapeutic seed  
7 according to a seventh embodiment of the invention;

8  
9        Figure 19 is an enlarged schematic longitudinal section of a  
10 radioactive therapeutic seed according to the seventh embodiment  
11 shown with a marker of a first length;

12  
13        Figure 20 is an enlarged schematic longitudinal section of a  
14 radioactive therapeutic seed according to an eighth embodiment  
15 shown with markers of a first length;

16  
17        Figure 21 is a view similar to Figure 20 in which the markers  
18 are drilled down to a second length; and

19  
20        Figure 22 is an enlarged schematic longitudinal section of a  
21 radioactive therapeutic seed according to a ninth embodiment shown  
22 with a marker of a first length.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Referring now to Figures 1 and 2, according to a first embodiment of the invention, a radioactive therapeutic seed 10 includes a preferably titanium capsule 12 defined by two halves 14, 16, each having a closed end 18, 20, an open end 22, 24, and an interior portion 26, 28. Each closed end 18, 20 is optionally provided with a connector 32 for connecting to a spacing link (not shown), as described in detail in co-owned U.S. Serial No. 09/312,215, hereby incorporated by reference herein in its entirety. In the interior portion 26, 28 of each half 14, 16 of the capsule 12, isotope bearing structures 34 are provided. Preferably, the isotope bearing structures 34 are one or more radiolucent particles, preferably made from titanium, aluminum or glass, and preferably spherically shaped. As used herein, the terms "radiotransparent", "radiolucent", "radiotranslucent", and "low Z material" are used interchangeably. The particles 34 are provided with a thin coating of silver over which a radioactive isotope 36 is provided. The two halves 14, 16 of the capsule are welded about a plug 38. The plug 38 is preferably a relatively thick titanium tube. A radiopaque marker 40 is provided axially in the plug 38. Additionally or alternatively, the plug 38 or marker 40 may be comprised of a diamagnetic substance, e.g., a gadolinium metal or salt, to permit visualization of the seed with

1 magnetic resonance imaging (MRI). The plug 38 and preferably the  
2 marker 40 are provided with a transverse preferably diametric bore  
3 42 capable of receiving a second radiopaque and/or MRI-visible  
4 marker. The plug 38 preferably includes tapered ends 44, 46 to  
5 facilitate positioning the open ends 22, 24 thereof, and a  
6 central circumferential ridge 48 against which the open ends of  
7 the two halves of the capsule are butt against and welded thereto.

8  
9       Turning now to Figures 3 and 4, a second radiopaque marker 50  
10 may be positioned in the bore 42 of the seed 10, thereby  
11 radiographically distinguishing a seed provided with the second  
12 marker relative to a seed not provided with the second marker;  
13 that is, a seed provided with solely the first marker 40 will have  
14 in one orientation a broken linear radiographic image (Fig. 2),  
15 while a seed provided with both the first marker 40 and second  
16 marker 50 will have in one orientation a cross-shaped radiographic  
17 image (Fig. 4). A system may thereby be provided which includes a  
18 plurality of seeds 10 and a plurality of second markers 50 for  
19 selective insertion into the seeds by a physician prior to  
20 implantation of the seeds into a patient. Alternatively, the  
21 seeds may be provided to the physician already divided into groups  
22 which are distinguishably radiographically marked; i.e., provided  
23 with and without second markers.

1 Referring now to Figures 5 and 6, a second embodiment of a  
2 therapeutic seed 110 according to the invention is shown. The  
3 seed 110 includes a radiolucent titanium capsule 112 defined by  
4 two halves 114, 116, each having a closed end 118, 120, optionally  
5 provided with a connector 132, an open end 122, 124, and an  
6 interior portion 126, 128. In the interior portion 126, 128 of  
7 each half 114, 116 of the capsule 112, a silver tube 134, 136 is  
8 provided. Each tube 134, 136 is preferably 0.025 inch in length  
9 and preferably has a wall thickness of .004 inch. The interior  
10 surfaces 138, 140 of the tubes are coated with I-125 or another  
11 radioisotope. As the tubes 134, 136 may be shorter than the  
12 length of the interior portion 126, 128, spacers 142, 144 may be  
13 provided in the interior portion to prevent relative movement of  
14 the tubes within the capsule 112. The two halves 114, 116 of the  
15 capsule are welded about a plug 146. The plug 146 is preferably a  
16 titanium tube having tapered ends 150, 152 to facilitate  
17 positioning the open ends 122, 124 thereover, and a central  
18 circumferential ridge 154 against which the open ends of the two  
19 halves of the capsule are butt against and welded thereto. A  
20 radiopaque marker 156 is provided in the plug 146. Additionally  
21 or alternatively, the marker 156 may be MRI-visible. The plug 146  
22 and the marker 156 are provided with a diametric bore 158  
23 accessible from the exterior of the seed 110. Turning now to  
24 Figures 7 and 8, the bore 158 may be provided with a second marker

1 160, as described above, to thereby radiographically distinguish  
2 seeds provided with and without second markers.

3  
4 Referring now to Figure 9, a third embodiment of a  
5 radioactive therapeutic seed according to the invention is shown.  
6 The seed 210 comprises a radioactive isotope 212 deposited on the  
7 outer surface of a hollow radiolucent tube 214. Optionally, a  
8 radiopaque band 216 may be centrally located on the outer surface  
9 of the tube 214, and the radioactive isotope 212 may then either  
10 extend over the entire outer surface of the tube 214, including  
11 over the band 216, or may be coated on the outer surface of the  
12 seed from the ends of the seed to areas adjacent the edges of the  
13 band. A biologically-compatible, radiolucent, surface-sealing  
14 layer 218 seals the external surface of the tube 214. The seed as  
15 described thus far is substantially similar to that disclosed in  
16 U.S. Patent No. 5,713,828 which is hereby incorporated by  
17 reference herein in its entirety. In accord with the invention, a  
18 radiopaque marker wire 220 is positioned in the hollow of the tube  
19 214, and where the seed is provided with a radiopaque band 216,  
20 the marker wire is preferably of a length different than the band.  
21 The length of the marker wire 220 may be selected to provide an  
22 indication of the level of radioactivity of the seed 210. For  
23 example, referring to Figure 10, a marker wire 220a relatively  
24 longer than marker wire 220 shown in Figure 9 may be used to

1 radiographically distinguish the seed shown in Figure 9 from the  
2 seed shown in Figure 10. It will be appreciated that, in accord  
3 with this embodiment, a system of seeds may be provided which  
4 includes at least two sets of seeds radiographically  
5 distinguishable from each other.

6  
7 With respect to the third embodiment, it will be appreciated  
8 that the marker wire may alternatively be a tubular marker 220b,  
9 thereby permitting the passage of a suture wire therethrough to  
10 couple the seed to the tissue at an implant site (Fig. 11). It  
11 will be further appreciated that multiple markers may be provided  
12 in the hollow of the tube, e.g., a tubular marker and a marker  
13 wire extending through the tubular marker. Additionally,  
14 transverse or diametric holes may be provided in the tube, and the  
15 marker wire may be positioned within with holes; i.e., the  
16 orientation of the second markers in the first and second  
17 embodiments. Furthermore, radiolucent plugs may be provided on  
18 either end of the marker wire or tubular marker to seal the seed  
19 about the markers.

20  
21 Turning now to Figure 12, a fourth embodiment of a  
22 therapeutic seed 310 according to the invention is shown. The  
23 seed 310, substantially as described with respect to the second  
24 embodiment, includes a radiolucent titanium capsule 312 welded

1 about a plug 346, and one or more tubes 334, 336 within the  
2 capsule having I-125 or another radioisotope coated on the  
3 interior surfaces 338, 340 of the tubes. A radiopaque marker 356  
4 is provided within the capsule. According to the fourth  
5 embodiment, the marker is a radiopaque material having a low  
6 melting point, e.g., an indium alloy, a bismuth alloy, or a solder  
7 or other eutectic, which is in solid form when the seed 310 is at  
8 body temperature. A heat-shrinkable or elastic sleeve 358 may be  
9 provided over the marker. Referring to Figure 13, when heat is  
10 applied to the seed 310, such that the seed is at a temperature  
11 greater than body temperature, the radiopaque material of the  
12 marker 356 melts and the sleeve 358 shrinks about the melted  
13 material, forcing at least some of the radiopaque material from  
14 the sleeve such that the marker 356 changes shape, e.g., forms a  
15 relatively longer bar-bell shape.

16  
17 It will be appreciated that in the fourth embodiment,  
18 otherwise like seeds which were made at different times, and  
19 therefore have different remaining useful life through which they  
20 may provide a therapeutic dose of radiation, may be separately  
21 identified and used together. For example, heat may be applied to  
22 a first set of relatively older seeds to cause their markers to be  
23 relatively longer than a second set of relatively newer seeds.

1 Once implanted, the position of the seeds may be individually  
2 monitored by distinguishing their respective markers.

3  
4 Referring now to Figure 14, a seed 410 used in the  
5 manufacture of a fifth embodiment of the invention is shown. The  
6 seed 410 includes an outer cylinder 412, a stepped inner cylinder  
7 (or inner device) 414, a band or carrier 416, and a radioactive  
8 isotope 418 coated on the carrier 416 about a portion of the  
9 stepped inner cylinder. The outer cylinder 412 and the inner  
10 cylinder 414 are made of radiotransparent, radiotranslucent, or  
11 low Z material which does not absorb much radiation. The outer  
12 cylinder 412 has a substantially constant diameter, a closed end  
13 420, and an open end 422. The stepped inner cylinder 414 has a  
14 reduced diameter portion 424 and an enlarged diameter portion 426.  
15 The band or carrier 416 is applied over the reduced diameter  
16 portion 424 such that the stepped inner cylinder 414 carries the  
17 band, as shown in Figure 14. For example, the band or carrier 416  
18 may be a resilient plastic band which includes a peripheral  
19 longitudinal slot (not shown) enabling the band to be opened and  
20 placed over the reduced diameter portion. As another example, the  
21 band 416 may be made from a deformable and preferably  
22 radiotransparent metal which may be bent about the reduced  
23 diameter portion 424 such that the band cannot be inadvertently  
24 released from the inner cylinder 414. Alternatively, the

1 radioisotope may be coated directly on the reduced diameter  
2 portion 424 of the stepped inner cylinder 414, with the cylinder  
3 acting as a carrier for the radioisotope.

4  
5 As shown in Figure 14, the enlarged diameter portion 426 of  
6 the inner cylinder 414 has an outer diameter which is  
7 substantially the same as the inner diameter of the open end of  
8 the outer cylinder 412. The seed 410 is sealed by placing the  
9 stepped inner cylinder 414 inside the outer cylinder 412 so that  
10 the enlarged diameter portion 426 of the inner cylinder 414  
11 engages with the open end 422 of the outer cylinder 412 as shown.  
12 The end 427 of the enlarged diameter portion 426 of the inner  
13 cylinder 414 is welded to the open end 422 of the outer cylinder  
14 412 as indicated by reference numeral 429. Likewise, the end 431  
15 of the enlarged diameter portion 428 of the inner cylinder 414 is  
16 welded to the open end 420 of the outer cylinder 412 as indicated  
17 by reference numeral 433. The wall thickness of the outer  
18 cylinder 412 is substantially constant and the enlarged diameter  
19 portion 426 of the inner cylinder 414 is preferably hollow with a  
20 wall thickness comparable to the wall thickness of the outer  
21 cylinder. The relative sizes of the outer and inner cylinders  
22 facilitate assembly of the seed 410 and permit a substantially  
23 isotropic radiation pattern.

1 Referring to Figure 15, once the seed 410 is formed, a  
2 longitudinal bore 434 is provided in the seed from one end of the  
3 seed, but does not create a throughbore; i.e., the bore 434 does  
4 not extend completely through the seed as the bore has a closed  
5 end 435. The bore 434 may be made by laser drilling, mechanical  
6 drilling or boring, or other means. A radiopaque marker 436 is  
7 then positioned in the bore 434, preferably substantially  
8 completely filling the bore.

9  
10 Then, referring to Figure 16, when it is necessary to  
11 distinguish a seed having one level of radioactivity from a seed  
12 having another level of radioactivity, a portion of the marker  
13 436a of seed 410a may be removed by drilling the marker down to a  
14 smaller size. Preferably, the marker 436a is drilled through both  
15 its ends 438a, 440a (and through the closed end of the bore) such  
16 that the remaining portion of the marker 436a is longitudinally  
17 centrally located within the bore to maintain a uniform radiation  
18 distribution pattern. Preferably, a seed with a relatively lower  
19 radioactivity is provided with the marker of relatively smaller  
20 size. The seeds are thereby easily distinguishable under  
21 fluoroscopy.

22  
23 Turning now to Figure 17, a sixth embodiment of a  
24 brachytherapy seed 510 according to the invention, substantially

1 similarly to the fifth embodiment (with like parts given numbers  
2 incremented by 100) is shown. The radioisotope is provided as a  
3 coating directly on the reduced diameter portion 524 of the  
4 stepped inner cylinder 514 (or inner device), and the seed is  
5 formed as an encapsulation as described above. Then, a  
6 longitudinal throughbore 534 is provided completely through the  
7 seed. The throughbore 534 may be made by laser drilling,  
8 mechanical drilling or boring, or other means. A radiopaque  
9 marker 536 is then positioned in the bore 534, preferably  
10 substantially completely filling the bore. The marker 536 may  
11 then be reduced in size by drilling the marker, preferably equal  
12 amounts from each end.

13

14 Referring now to Figures 18 and 19, a seed substantially as  
15 described above with respect to the sixth embodiment is  
16 manufactured in a different manner according to a seventh  
17 embodiment of the invention. First, a stepped inner cylinder 614  
18 having a central reduced diameter portion 624 is provided with a  
19 longitudinal throughbore 634. A radiopaque marker 636 is provided  
20 in the throughbore 634 (as shown in Fig. 18). Alternatively, the  
21 inner cylinder is formed about the marker, for example, by bending  
22 a suitable material about the marker to form the inner cylinder.  
23 Next, the reduced diameter portion 624 of the inner cylinder 614  
24 is coated or otherwise provided with the radioisotope 618. Then,

1 referring particularly to Figure 19, the outer cylinder 612 is  
2 provided about the inner cylinder 614 and the ends of the inner  
3 and outer cylinders are sealed together, e.g., by welding, to form  
4 the seed encapsulation 610. The marker 636 of the seed 610 may  
5 then be longitudinally drilled, preferably at each end of the seed  
6 (as described above with respect to Fig. 16), to remove equal  
7 amounts of the marker and thereby reduce the size of the marker.

8  
9 Turning now to Figure 20, a seed 710 according to an eighth  
10 embodiment of the invention is shown. The seed 710 includes an  
11 outer cylinder 712, first and second stepped inner members 714,  
12 715 (together forming an inner device) each having a reduced  
13 diameter portion 724, 725 and an enlarged diameter portion 726,  
14 727, markers 736, 737, a band or carrier 716, and a radioactive  
15 isotope 718 carried by the band 716 about the reduced diameter  
16 portions of the stepped inner members 714, 715. The inner members  
17 714, 715 include externally directed bores 734, 735, and the  
18 markers 736, 737 are provided in the bores 734, 735. The outer  
19 cylinder 712 and the inner portions 714, 715 are made of a low Z  
20 material which does not absorb much radiation. The radioisotope  
21 718 is preferably provided on a cylindrical band 716, and the  
22 reduced diameter portions 724, 725 of the stepped inner members  
23 714, 715 are inserted into opposite ends of the band 716.  
24 Alternatively, the radioisotope may be coated directly on the

1 reduced diameter portions 724, 725 of the stepped inner members  
2 714, 715 (inner device). The seed 710 is sealed by placing the  
3 stepped inner members 714, 715 inside the outer cylinder 712 so  
4 that the enlarged diameter portion 726, 727 of the inner members  
5 714, 715 engage with the open ends 722, 723 of the outer cylinder  
6 712, and are welded together. The markers 736, 737 may be altered  
7 in size by longitudinally drilling the markers at 740, 741 and  
8 into the bores 734, 735 as described above and as shown in Figure  
9 21.

10  
11 Referring now to Figure 22, a seed 810 according to a ninth  
12 embodiment of the invention and substantially similar to the  
13 eighth embodiment (with like parts having numbers incremented by  
14 100 relative thereto) is shown. The distinguishing feature  
15 relative to the eighth embodiment is that each stepped inner  
16 member 824, 825 includes a medially directed bore 834, 835 and  
17 preferably a single marker 836 extends within the bores. The  
18 marker 836 of the seed may altered in size by drilling through the  
19 closed ends 842, 843 of the inner member, into the bores 834, 835  
20 and into the marker 836.

21  
22 Each embodiment permits at least two groups of seeds to be  
23 radiographically distinguished from one another by the use of  
24 differing marker configurations. Each embodiment is further

1 capable of being selectively configured by the physician prior to  
2 implantation of the seeds, or by the manufacturer for delivery to  
3 the physician in radiographically distinguishable sets. As a  
4 result, seeds having different levels of radiation emission can be  
5 distinguished in vivo and their effect monitored by the physician.  
6 This is particularly useful in that the invention permits discrete  
7 monitoring of two or more sets of seeds, e.g., seeds having  
8 relatively different levels of radiation, seeds having relatively  
9 different radiation distribution, or seeds having radioactive  
10 isotopes with relatively different half-lives, as each set may be  
11 radiographically distinct. In addition, it will be appreciated  
12 that the provision of a second marker to each embodiment does not  
13 detrimentally affect the relatively isotropic distribution of the  
14 seeds.

15  
16 There have been described and illustrated herein several  
17 embodiments of a radioactive therapeutic seed. While particular  
18 embodiments of the invention have been described, it is not  
19 intended that the invention be limited thereto, as it is intended  
20 that the invention be as broad in scope as the art will allow and  
21 that the specification be read likewise. For example, those  
22 skilled in the art will appreciate that certain features of one  
23 embodiment may be combined with features of another embodiment to  
24 provide yet additional embodiments. It will be appreciated that

1 numerous other seed designs may be configured to receive a  
2 secondary marker or to permit marker alteration to thereby permit  
3 relative seed differentiation, and that the particular designs  
4 disclosed herein are only exemplary. In addition, while the  
5 second marker, in the first and second embodiments, the marker  
6 wire in the third embodiment, or the markers in the fourth through  
7 ninth embodiments, have been described as being radiopaque, it  
8 will be appreciated that such markers may be MRI-visible.  
9 Likewise, while the first marker or marker band has been described  
10 as being radiopaque, each may be MRI-visible, and the second  
11 marker and marker wire may be radiopaque. Also, while the second  
12 marker in the first and second embodiments has been described as  
13 preferably being diametrically and/or transversely oriented, it  
14 will be appreciated that the second marker need only be angled  
15 relative to the first marker or non-axial relative to the  
16 longitudinal axis of the capsule. In addition, the wire marker in  
17 the third embodiment may be cylindrical or an elongate rectangular  
18 shape, each being substantially a wire at the scale of  
19 brachytherapy seeds. Furthermore, while capsules in particular  
20 embodiments are preferably formed from two halves (for purposes of  
21 isotropic radiation distribution), it will be appreciated that the  
22 two parts forming the capsule need not be halves, e.g., one part  
23 being one third the length of the capsule and the other part begin  
24 two thirds the length of the capsule. Moreover, while in

1   embodiments one through four, the isotope bearing surface has been  
2   disclosed as the outer surface in particular embodiments and the  
3   inner surface in other embodiments, it will be appreciated that  
4   either of the inner and outer surfaces may be used as the isotope  
5   bearing surface, though it is believed that the embodiments as  
6   described provide the most isotropic radiation distribution. In  
7   addition, while a particular seed has been disclosed having a  
8   marker which changes shape when energy is applied to the seed, it  
9   will be appreciated that such markers may be used in seeds having  
10   different radioisotope bearing elements and different capsule  
11   configurations. Also while a meltable marker has been described  
12   having a heat shrinkable or elastic sleeve thereabout, it will be  
13   appreciated that the sleeve is not required, and that the marker  
14   can be altered from a defined shape, e.g., cylindrical, to an  
15   amorphous configuration upon melting. Further, where a sleeve is  
16   used, it will be appreciated that the marker after heating, if  
17   substantially melted, may take the configuration of two or more  
18   separated masses. In addition, while in the fifth through ninth  
19   embodiments, markers having an outer diameter substantially the  
20   same size as the inner diameter of bore are shown, it will be  
21   appreciated that markers of a relatively smaller diameter may be  
22   used and that the open end or ends of the bore may be capped to  
23   retain the marker. Furthermore, in the fifth through ninth  
24   embodiments, while marker size reduction is disclosed, it will be

1 appreciated that a first marker having a length substantially half  
2 that of the bore may be centrally provided within the bore, and  
3 then a second marker of substantially the same size may be  
4 inserted into the bore to slide over the first marker and  
5 substantially completely fill the bore to thereby distinguish the  
6 seed with an imaging device. It will therefore be appreciated by  
7 those skilled in the art that yet other modifications could be  
8 made to the provided invention without deviating from its spirit  
9 and scope as claimed.